Patient- and Caregiver-Reported Experiences of Hyperphagia in Bardet-Biedl Syndrome Before and During Setmelanotide Treatment

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Summary

- **Both patients with Bardet-Biedl syndrome (BBS) and their caregivers reported that hyperphagia had broad, negative impacts on quality of life including emotional and physical impairment, difficulties with concentration/focus, and strained relationships**
- **All interview participants experienced or observed notable improvements in hyperphagia during setmelanotide treatment, resulting in meaningful improvements in physical and emotional well-being for both patients and caregivers**
- **The results of this study exemplify the usefulness and importance of the US Food and Drug Administration recommendation[1] to utilize patient experience data to further elucidate the findings in quantitative clinical trials**
- **These interviews consistently demonstrated that reductions in both hunger and weight (as quantified in Phase 3 trials of setmelanotide) were incredibly meaningful to both patients and caregivers, as these changes led to substantial improvements in overall physical and emotional well-being**

Introduction

- BBS is a rare genetic disease associated with hyperphagia, a pathologic insatiable hunger due to impaired signaling in the energy-regulating melanocortin-4 receptor (MC4R) pathway that often manifests in early-onset, severe obesity[2,3]
- Although research in this area is limited, studies have shown the impacts of BBS are distressing for both patients and their caregivers, affecting not only physical health and functioning but also psychosocial functioning and finances[3,4]
- In this study, we characterize the nature, severity, and effect of hyperphagia on patients and caregivers before and during treatment with setmelanotide

Methods

- In-depth qualitative interviews were conducted with patients and caregivers of patients with BBS who previously participated in a Phase 2 or 3 clinical trial of the MC4R agonist setmelanotide (NCT03013543 or NCT03746522)[3,5,6]
- Participants were interviewed via telephone between March and June 2021 using a semistructured interview guide to explore the patient experience with and caregiver observations of behaviors associated with hyperphagia both before and during setmelanotide treatment
- Interview transcripts were analyzed using a thematic approach

Results

Patient Characteristics

- A total of 19 telephone interviews were conducted (8 patients and 11 caregivers)
- The average age of patient participants was 36 years, and the average age of the patients associated with caregivers was 16 years; most patients were female (Table 1)
- All 11 caregivers were female (ie, the patient's mother)

Table 1. Baseline Patient Characteristics

	Patients (N=19)[a]
Age, mean (range), years	
Self-reported patients (n=8)	36 (17-65)
Caregiver-reported patients (n=11)	16 (7-36)
Sex, n (%)	
Female	12 (63.2)
Male	7 (36.8)
Time since first clinical trial, mean (range), months	
Self-reported patients	29 (12-48)
Caregiver-reported patients	24 (8-40)

[a]This includes both self-reported patients (n=8) and caregiver-reported patients (n=11).

Patient Experience Prior to Setmelanotide Treatment

- Before setmelanotide treatment, all participants described their (or their child's) hunger as all-consuming, leading to an obsessive focus on food (Table 2)
- The majority of participants (5 patients, 10 caregivers) reported a complete lack of control related to eating
  - Of these participants, 9 reported intense, unrelenting hunger that never waned
- Negative impacts on patients' lives included decrements in emotional well-being, difficulties with concentration that diminished school performance, and impaired relationships with siblings and caregivers
- Caregivers reported constant concern for their child's health and stress about managing food-seeking behaviors
- Both patients and caregivers experienced or observed emotional effects of hyperphagia that included sadness, frustration, irritability, anxiety, and feelings of guilt

Table 2. Patient- and Caregiver-Reported Experiences of Hunger, Eating Habits, and Effect of Hyperphagia Before Treatment With Setmelanotide

Before Setmelanotide Treatment

Feelings of hunger	Eating habits	Effect of hyperphagia on patients	Effect of hyperphagia on caregivers
"I was always hungry. And if I didn't eat when I needed to, I would be very unhappy. Couldn't wait to eat." – Patient	*"I was eating pretty much whatever, whenever and wasn't able to stop myself from eating or sneaking food in the middle of the night."* – Patient	*"I felt very agitated and very sad a lot of the time... I just really didn't have many friends, really even many friends to hang out with and…I don't know. I just kind of felt alone in a sense."* – Patient	*"Yeah, we didn't like to go places. And if you go to somebody's house, trying to keep them away from the chips and dip is so hard, it's easier to just not go."* – Caregiver
"She was hungry all the time, and it was a relentless hunger. She would eat everything on her plate and everything on my plate, and anything she could find." – Caregiver	*"He would eat until he was physically hurting. And then in the same breath, tell us that he was hurting and asked for a snack or something to eat. He'd sneak food. He would troll people for food, stalk people with food."* – Caregiver	*"She couldn't do as well in school because she was thinking about what was in her lunchbox or what she was going to get at lunch or when she could eat it or how soon to lunch. It really did, it was very obsessive the amount of thoughts about the timing of food."* – Caregiver	*"It mostly affected me emotionally because I constantly felt like I was failing. It was like a no-win situation because if I did not give her extra food, then I felt terrible for denying her that when I knew she felt like she was starving, and if I did give it to her, I felt like I was slowly killing her and causing her health problems."* – Caregiver

Patient- and Caregiver-Reported Changes With Setmelanotide Treatment

- All participants experienced or observed notable improvements in hyperphagia during treatment with setmelanotide (Table 3)
  - The most important improvements related to hunger reduction included better health and weight loss, as well as a decrease in obsessive focus on food and food-seeking behaviors (Table 4)
- All participants reported improvements in how they felt (physically and/or emotionally), and generally reported high levels of satisfaction with and a strong desire to continue setmelanotide (Table 5)

Table 3. Patient- and Caregiver-Reported Experiences of Hunger, Eating Habits, and Effect of Hyperphagia During Treatment With Setmelanotide

After Setmelanotide Treatment

Feelings of hunger	Eating habits	Effect of hyperphagia on patients	Effect of hyperphagia on caregivers
"I feel great. I feel satisfied. I feel full when I'm done eating. Sometimes, I won't eat everything that's on my plate." – Patient	*"I feel like I've had a lot more willpower since I've been on the medication, and I feel like I haven't really been tempted to grab really anything during meals, which has felt good."* – Patient	*"It made me more positive and more peppy, my voice and thinking and wanting to be out more with people."* – Patient	*"Well, it's just a lot easier because I don't have to be the food police anymore…. It's like everything in the house is more laid back instead of being on edge about food."* – Caregiver
"After we started this setmelanotide trial, she told me for the first time that she had no idea what it was not to be hungry. So that was really sad. So before the trial, I guess, according to her, she had never experienced not being hungry before…." – Caregiver	*"I find that she makes a lot of better choices since she's been on setmelanotide, willingly. I don't have to…she packs her lunch and she knows my rules. You have to have a veggie, fruits, and then a yogurt. But often she would try…before, she would try to sneak other things in there or put more. But now she makes her own lunch and when I look in it, it's all healthy."* – Caregiver	*"I think it has helped. Not that he had a mood problem but I think he is happy that he knows he can control things himself, that this has empowered him to make life choices and they're the good choices. I'm sure that's given him some confidence."* – Caregiver	*"It just affected us so much. Obviously, as a parent, you worry so much about your kids and when something like that drastic changes, it's pretty freeing and pretty amazing. Even my husband and I, our relationship together, because we were always so worried about it. It really helped us to be able to calm down and not be so stressed out."* – Caregiver

Table 4. Most Important Improvement to Patients in Clinical Trials With Setmelanotide

Improvement, n	Patient reported (n=8)	Caregiver reported (n=11)	Total (N=19)[a]
Weight (able to eat less) and general health	5	6	11
Decrease in obsessive focus on food/hunger	3	5	8
Increase in energy	1	2	3
More social/interactions with friends/family	3	—	3
Physical ability	—	2	2
Better mood/happier	—	2	2
Greater control over food	1	—	1

[a]Some patients and caregivers reported >1 most important improvement, thus the total number included is >19.

Table 5. Patient- and Caregiver-Reported Meaningfulness of Improvements in Hunger, Overall Satisfaction of Treatment, and Feelings if Treatment Were Discontinued

Meaningfulness	Overall satisfaction	Discontinuing setmelanotide
"Oh gosh. Well, I feel like I've had more positive interactions with people not revolving around the weight…. I think just, whether it was family or friends, whoever, realizing that this actually was working and that it was making an impact on my life." – Patient	*"I'm very satisfied with the medication because it has helped me be more aware of food and what I'm eating or what the medication is telling my brain or helping me lose weight."* – Patient	*"Oh, I would feel very distraught and very disappointed and just not myself.... Because I've lost so much weight, and people have recognized how hard I've been trying to work on that. And I also have a therapist who I've also been working on some mental stuff. And I think it's just…I think it would affect all of it."* – Patient
"It gives me the hope for the future that he's going to be a secure, independent person, even if he lives with his sister or if he lives with a caretaker. He's going to be healthy and he's going to live longer, for sure." – Caregiver	*"Because I literally feel like it's saved her life or going to save her life because…I don't know. I feel eternally grateful to have been able to get her in this and for everything that they've done for her and the medicine. Absolutely very thankful."* – Caregiver	*"I would be devastated. And that's one of my biggest fears. Because I feel like it would be taking away all our hope. Before we started this trial, I literally felt hopeless, like there was nothing I can do, like it was completely out of my control…. And if it was taken away, I would feel like it would literally be a death sentence."* – Caregiver

Conclusions

- This study confirms that hyperphagia imposes a broad and major burden on both patients with BBS and their caregivers
- Treatment with setmelanotide facilitated major improvements in hyperphagia and promoted substantial and meaningful changes in the patients' behaviors, their life experiences, and the life experiences of the caregivers
- The results of these interviews enhance the findings from previous clinical trials and emphasize that disrupting hyperphagia through pharmacologic intervention can improve overall health and emotional well-being (for both the patient and caregiver) as well as minimize the impact of hyperphagia on school performance, productivity, and family dynamics

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